WHAT IS CLAIMED IS:

1. An isolated or recombinant polypeptide comprising an extracellular domain sequence, wherein said extracellular domain sequence has at least about 75% amino acid sequence identity to an extracellular domain sequence of at least one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, and is not a naturally-occurring extracellular domain sequence, and wherein said polypeptide has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

2. The isolated or recombinant polypeptide of claim 1, wherein said extracellular domain sequence has at least about 90% sequence identity to an extracellular domain sequence of at least one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

3. The isolated or recombinant polypeptide of claim 1, which polypeptide comprises an extracellular domain sequence of any one of SEQ ID NOS:48-68, 174-182, 184-221, 283-285, and 290-293.

4. The isolated or recombinant polypeptide of claim 1, which polypeptide comprises an amino acid sequence of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

5. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide has a CD28/CTLA-4 binding affinity ratio greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

6. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide has either a same binding affinity or an enhanced binding affinity for CD28 as compared to a binding affinity of a wild type co-stimulatory molecule for CD28.

7. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide has a decreased or a lowered binding affinity for CTLA-4 as compared to a binding affinity of a wild type co-stimulatory molecule for CTLA-4.

8. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide induces T-cell proliferation or T-cell activation or both T-cell proliferation and T-cell activation.

9. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide induces T-cell proliferation.

10. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide induces a T-cell proliferative response equal to or greater than that of human B7-1.

11. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide modulates T-cell activation, but does not induce proliferation of purified T-cells activated by soluble anti-CD3 mAbs.

12. The isolated or recombinant polypeptide of claim 5, which polypeptide comprises an extracellular domain sequence of any one of SEQ ID NOS:48-68 and 174-209.

13. The isolated or recombinant polypeptide of claim 1, which polypeptide comprises an extracellular domain sequence encoded by a coding polynucleotide sequence, the coding polynucleotide sequence selected from the group of:

(a) an extracellular domain coding sequence of a polynucleotide sequence selected from any of SEQ ID NOS:1-21 and 95-142;

(b) an polynucleotide sequence that encodes the extracellular domain of a polypeptide selected from any of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293; and

(c) a polynucleotide sequence which hybridizes under stringent conditions over substantially the entire length of a polynucleotide sequence (a) or (b).

14. An isolated or recombinant polypeptide, which polypeptide comprises a non-naturally-occurring amino acid sequence encoded by a nucleic acid comprising a polynucleotide sequence selected from the group of:

(a) a polynucleotide sequence selected from SEQ ID NOS:1-21 and 95-142, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which hybridizes under highly stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b);

(d) a polynucleotide sequence comprising all or a fragment of (a), (b), or (c), wherein the fragment encodes a polypeptide having a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1;

(e) a polynucleotide sequence encoding a polypeptide, the polypeptide comprising an amino acid sequence which is substantially identical over at least about 150 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293; and

(f) a polynucleotide sequence encoding a polypeptide that has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1, which polynucleotide sequence has at least about 70% identity to at least one polynucleotide sequence of (a), (b), (c), or (d).

15. The isolated or recombinant polypeptide of claim 14, the polypeptide comprising an amino acid sequence of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

16. The isolated or recombinant polypeptide of claim 14, wherein the polypeptide has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

17. The isolated or recombinant polypeptide of claim 14, wherein the polypeptide induces T-cell proliferation.

18. The isolated or recombinant polypeptide of claim 14, wherein the polypeptide induces a T-cell proliferative response equal to or greater than that of human B7-1.

19. An isolated or recombinant polypeptide comprising a sequence according to the formula:

MGHTM-X6-W-X8-SLPPK-X14-PCL-X18-X19-X20-QLLVLT-X27-LFYFCSGITPKSVTKRVKETVMLSCDY-X55-TSTE-X60-LTSLRIYW-X69-KDSKMVLAILPGKVQVWPEYKNRTITDMNDN-X101-RIVI-X106-ALR-X110-SD-X113-GTYTCV-X120-QKP-X124-LKGAYKLEHL-X135-SVRLMIRADFPVP-X149-X150-X151-DLGNPSPNIRRLICS-X167-X168-X169-GFPRPHL-X177-WLENGEELNATNTT-X192-SQDP-X197-T-X199-LYMISSEL-X208-FNVTNN-X215-SI-X218-CLIKYGEL-X227-VSQIFPWSKPKQEPPIDQLPF-X249-VIIPVSGALVL-X261-A-X263-VLY-X267-X268-ACRH-X273-ARWKRTRRNEETVGTE RLSPIYLGSAQSSG (SEQ ID NO:284), or a subsequence thereof comprising the extracellular domain, wherein

position X6 is Lys or Glu; position X8 is Arg or Gly; position X14 is Arg or Cys; position X18 is Trp or Arg; position X19 is Pro or Leu; position X20 is Ser or Pro; position X27 is Asp or Gly; position X55 is Asn or Ser; position X60 is Glu or Lys; position X69 is Gln or Arg; position X101 is Pro or Leu; position X106 is Leu or Gln; position X110 is Pro or Leu; position X113 is Lys or Ser; position X120 is Val or Ile; position X124 is Val or Asp; position X135 is Thr or Ala; position X149 is Thr, Ser, or del; position X150 is Ile or del; position X151 is Asn or Thr; position X167 is Thr or del; position X169 is Ser or del; position X169 is Gly or del; position X177 is Cys or Tyr;

position X192 is Val or Leu; position X197 is Gly or Glu; position X199 is Glu or Lys; position X208 is Gly or Asp; position X215 is His or Arg; position X218 is Ala or Val; position X227 is Ser or Leu; position X249 is Trp, Leu, or Arg; position X261 is Ala or Thr; position X263 is Val, Ala, or Ile; position X267 is Arg or Cys; position X268 is Pro or Leu; and position X273 is Gly or Val.

20. The isolated or recombinant polypeptide of claim 19, which polypeptide comprises an extracellular domain sequence of any one of SEQ ID NOS:51-56, 58, 61, 66, 67, 174-179, 181, 185-187, 189, 192-194, 197, 199, 202, 205, 208, 215, 217, 220, and 285.

21. The isolated or recombinant polypeptide of claim 19, wherein the polypeptide has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

22. The isolated or recombinant polypeptide of claim 19, wherein the polypeptide induces T-cell proliferation.

23. The isolated or recombinant polypeptide of claim 19, wherein the polypeptide induces a T-cell proliferative response equal to or greater than that of human B7-1.

24. The isolated or recombinant polypeptide of claim 19, comprising three or more of: Lys at position X6; Arg at position X8; Arg at position X14; Trp at position X18; Pro at position X19; Ser at position X20; Asp at position X27; Asn at position X55; Leu at position X106; Pro at position X110; Lys at position X113; Val at position X120; Val at position X124; Thr at position X135; Asn at position X151; Cys at position X177; Val at position X192; Gly at position X197; Glu at position X199; Gly at position X208; His at position X215; Ala at position X218; Trp at position X249; Ala at position X261; Val at position X263; Arg at position X267; Pro at position X268; and Gly at position X273.

25. The isolated or recombinant polypeptide of claim 24, comprising three or more of: Arg at position X8; Arg at position X14; Trp at position X18; Pro at position X19; Ser at position X20; Pro at position X110; Val at position X120; Val at position X124; Cys at position X177; Val at position X192; Gly at position X197; Glu at position X199; Gly at position X208; His at position X215; Ala at position X218; Trp at position X249; Ala at position X261; and Val at position X263.

26. The isolated or recombinant polypeptide of claim 25, comprising the extracellular domain sequence of SEQ ID NO:66 or SEQ ID NO:285.

27. The isolated or recombinant polypeptide of claim 25, comprising the sequence SEQ ID NO:66 or SEQ ID NO:285.

28. An isolated or recombinant polypeptide comprising a subsequence of an amino acid sequence set forth in any of SEQ ID NOS:48-68, 174-182, 184-221, 283-285, and 290-293, wherein the subsequence is the extracellular domain of said amino acid sequence.

29. The isolated or recombinant polypeptide of claim 1, 14, 19, or 28, comprising a signal sequence.

30. The polypeptide of claim 1, 14, 19, or 28, wherein the signal sequence is selected from the signal sequence set forth in any of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

31. The polypeptide of claim 1, 14, 19, or 28, comprising a transmembrane domain sequence or a cytoplasmic domain sequence selected from the transmembrane domain sequence or the cytoplasmic domain sequence set forth in any of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

32. The polypeptide of claim 1, 14, 19, or 28 comprising a soluble extracellular domain of a NCSM or a fragment or subsequence thereof.

33. The polypeptide of claim 1, 14, 19, or 28, wherein the polypeptide comprises a fusion protein comprising at least one additional amino acid sequence.

34. The polypeptide of claim 33, wherein the at least one additional amino acid sequence comprises an Ig polypeptide.

35. The polypeptide of claim 34, wherein the Ig polypeptide is a human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

36. The polypeptide of claim 1, 14, 19, or 28, comprising a polypeptide purification subsequence.

37. The polypeptide of claim 36, wherein the polypeptide purification subsequence is selected from: an epitope tag, a FLAG tag, a polyhistidine sequence, and a GST fusion.

38. The polypeptide of claim 1, 14, 19, or 28, comprising a modified amino acid.

39. The polypeptide of claim 38, wherein the modified amino acid is selected from: a glycosylated amino acid, a PEGylated amino acid, a farnesylated amino acid, an acetylated amino acid, a biotinylated amino acid, an amino acid conjugated to a lipid moiety, and an amino acid conjugated to an organic derivatizing agent.

40. A composition comprising at least one polypeptide of claim 38 and a pharmaceutically acceptable excipient.

41. A composition comprising at least one polypeptide of claim 1, 14, 19, or 28, and a pharmaceutically acceptable excipient.

42. A composition comprising:

an isolated or recombinant NCSM polypeptide comprising the amino acid sequence SEQ ID NOS:48-68, 174-221, 283-285, 290-293, or a costimulatory fragment thereof, wherein said costimulatory fragment has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1, and

a carrier.

43. An isolated or recombinant nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NOS:1-21 and 95-142, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which hybridizes under highly stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b); and

(d) a polynucleotide sequence comprising all or a fragment of (a), (b), or (c), wherein the fragment encodes a polypeptide having a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

44. An isolated or recombinant nucleic acid comprising a polynucleotide sequence encoding a polypeptide, wherein the encoded polypeptide comprises an amino acid sequence which is (a) substantially identical over at least about 150 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293 and (b) is a non naturally-occurring sequence.

45. The nucleic acid of claim 44, wherein the encoded polypeptide is substantially identical over at least about 175 contiguous amino acid residues of any one of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293.

46. An isolated or recombinant nucleic acid comprising a nucleotide sequence coding for a polypeptide comprising the amino acid sequence set forth in any of SEQ ID NOS:48-68, 174-221, 283-285, and 290-293, or a subsequence thereof, wherein the subsequence comprises at least one of: the signal sequence of said polypeptide, the extracellular domain of said polypeptide, the transmembrane domain of said polypeptide, and the cytoplasmic domain of said polypeptide, and wherein the amino acid sequence or subsequence is a non naturally-occurring sequence.

47. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1.

48. The nucleic acid of claim 43, 44, or 46, wherein the polypeptide has either a same binding affinity or an enhanced binding affinity for CD28 as compared to a binding affinity of a wild type co-stimulatory molecule for CD28.

49. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide has a decreased or a lowered binding affinity for CTLA-4 as compared to a binding affinity of a wild type co-stimulatory molecule for CTLA-4.

50. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide induces T-cell proliferation or T-cell activation or both T-cell proliferation and T-cell activation.

51. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide modulates T-cell activation, but does not induce proliferation of purified T-cells activated by soluble anti-CD3 mAbs.

52. The nucleic acid of claim 43, 44, or 46, wherein the nucleic acid encodes a fusion protein comprising at least one additional amino acid sequence.

53. The nucleic acid of claim 52, wherein the at least one additional amino acid sequence comprises an Ig polypeptide.

54. The nucleic acid of claim 53, wherein the Ig polypeptide is a human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

55. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises a signal sequence.

56. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises a precursor peptide.

57. The nucleic acid of claim 43, 44, or 46, wherein the encoded polypeptide comprises an epitope tag sequence.

58. A cell comprising the nucleic acid of claim 43, 44, or 46.

59. The cell of claim 58, wherein the cell expresses a polypeptide encoded by the nucleic acid.

60. A vector comprising the nucleic acid of claim 43, 44, or 46.

61. The vector of claim 60, wherein the vector comprises a plasmid, a cosmid, a phage, a virus, or a fragment of a virus.

62. The vector of claim 60, wherein the vector is an expression vector.

63. The expression vector of claim 62, wherein the nucleic acid is operably linked to a promoter.

64. The expression vector of claim 62, further comprising a polynucleotide sequence encoding an antigen.

65. The expression vector of claim 64, wherein the antigen is a cancer antigen.

66. The expression vector of claim 64, wherein the nucleic acid is operably linked to first promoter and the polynucleotide sequence encoding the antigen is operably linked to a second promoter.

67. The expression vector of claim 65, wherein the cancer antigen is EpCam/KSA.

68. The expression vector of claim 67, wherein the expression vector comprises the vector shown in Figure 22B.

69. A host cell comprising the vector of claim 60.

70. A composition comprising the nucleic acid of claim 43, 44, or 46 and an excipient.

71. The composition of claim 70, wherein the excipient is a pharmaceutically acceptable excipient.

72. A composition of matter comprising at least one nucleic acid of claim 43, 44, or 46.

73. The composition of claim 72, wherein the composition comprises a library comprising at least about 2, 5, 10, 50 or more nucleic acids.

74. A composition produced by cleaving at least one nucleic acid of claim 43, 44, or 46.

75. The composition of claim 74, wherein the cleaving comprises mechanical, chemical, or enzymatic cleavage.

76. The composition of claim 75, wherein the enzymatic cleavage comprises cleavage with a restriction endonuclease, an RNAse, or a DNAse.

77. A composition produced by a process comprising incubating at least one nucleic acid of claim 43, 44, or 46 in the presence of deoxyribonucleotide triphosphates and a nucleic acid polymerase.

78. The composition of claim 77, wherein the nucleic acid polymerase is a thermostable polymerase.

79. An isolated or recombinant nucleic acid encoding a polypeptide that has a CD28/CTLA-4 binding affinity ratio equal to or greater than the CD28/CTLA-4 binding affinity ratio of human B7-1, produced by mutating or recombining at least one nucleic acid of claim 43, 44, or 46.

80. An isolated or recombinant polypeptide comprising a sequence having at least about 95% identity to at least about one of SEQ ID NOS:69-92, 222-252, 286-289, or a subsequence thereof comprising the extracellular domain, wherein said sequence (a) is a non naturally-occurring sequence, and (b) comprises at least one of:

Gly at position 2; Thr at position 4; Arg at position 5; Gly at position 8; Pro at position 12; Met at position 25; Cys at position 27; Pro at position 29; Leu at position 31; Arg at position 40; Leu at position 52; His at position 65; Ser at position 78;

Asp at position 80; Tyr at position 87; Lys at position 120; Asp at position 122; Lys at position 129; Met at position 135; Phe at position 150; Ile at position 160; Ala at position 164; His at position 172; Phe at position 174; Leu at position 176; Asn at position 178; Asn at position 186; Glu at position 194; Gly at position 196; Thr at position 199; Ala at position 210; His at position 212; Arg at position 219; Pro at position 234; Asn at position 241; Leu at position 244; Thr at position 250; Ala at position 254; Tyr at position 265; Arg at position 266; Glu at position 273; Lys at position 275; Ser at position 276; an amino acid deletion at position 276; or Thr at position 279, wherein the position number corresponds to that of the human B7-1 amino acid sequence (SEQ ID NO:278),

wherein said polypeptide has a CTLA-4/CD28BP binding affinity ratio equal to or greater than the CTLA-4/CD28BP binding affinity ratio of human B7-1.

81. The isolated or recombinant polypeptide of claim 80, wherein said polypeptide comprises a sequence having at least about 98% identity to at least one of SEQ ID NOS:69-92, 222-252, 286-289, or a subsequence thereof comprising the extracellular domain, said sequence comprising at least one of:

Gly at position 2; Thr at position 4; Arg at position 5; Gly at position 8; Pro at position 12; Met at position 25; Cys at position 27; Pro at position 29; Leu at position 31; Arg at position 40; Leu at position 52; His at position 65; Ser at position 78; Asp at position 80; Tyr at position 87; Lys at position 120; Asp at position 122; Lys at position 129; Met at position 135; Phe at position 150; Ile at position 160; Ala at position 164; His at position 172; Phe at position 174; Leu at position 176; Asn at position 178; Asn at position 186; Glu at position 194; Gly at position 196; Thr at position 199; Ala at position 210; His at position 212; Arg at position 219; Pro at position 234; Asn at position 241; Leu at position 244; Thr at position 250; Ala at position 254; Tyr at position 265; Arg at position 266; Glu at position 273; Lys at position 275; Ser at position 276; an amino acid deletion at position 276; and Thr at position 279, wherein the position number corresponds to that of the human B7-1 amino acid sequence (SEQ ID NO:278).

82. The isolated or recombinant polypeptide of claim 80, wherein said polypeptide comprises a sequence having at least about 98% identity to at least one of SEQ ID NOS:69-92, 222-252, and 286-289, said sequence comprising at least one of :

Gly at position 2; Gly at position 8; Cys at position 27; His at position 65; Asp at position 80; Asp at position 122; Met at position 135; Phe at position 150; Ala at position 164; Phe at position 174; Asn at position 186; Glu at position 194; Arg at position 219; Thr at position 250; Arg at position 266; Lys at position 275; and Ser at position 276, wherein the amino acid position numbers correspond to that of the human B7-1 amino acid sequence (SEQ ID NO:278).

83. The isolated or recombinant polypeptide of claim 80, wherein said polypeptide comprises a sequence having at least about 98% identity to the extracellular domain of at least one of SEQ ID NOS:69-92, 222-252, and 286-289, said sequence comprising at least one of :

His at position 65; Asp at position 80; Asp at position 122; Met at position 135; Phe at position 150; Ala at position 164; Phe at position 174; Asn at position 186; Glu at position 194; and Arg at position 219, wherein the amino acid position numbers correspond to that of the human B7-1 amino acid sequence (SEQ ID NO:278).

84. The isolated or recombinant polypeptide of claim 83, wherein said polypeptide comprises a sequence having at least about 98% identity to the extracellular domain of at least one of SEQ ID NOS:69-92, 222-252, 286-289, said sequence comprising at least two of :

His at position 65; Asp at position 80; Asp at position 122; Met at position 135; Phe at position 150; Ala at position 164; Phe at position 174; Asn at position 186; Glu at position 194; and Arg at position 219, wherein the amino acid position numbers correspond to that of the human B7-1 amino acid sequence (SEQ ID NO:278).

85. The isolated or recombinant polypeptide of claim 84, wherein said polypeptide comprises an extracellular domain of any one of SEQ ID NOS:81, 85, 86, 88, 90, and 91.

86. The isolated or recombinant polypeptide of claim 80, which polypeptide comprises an extracellular domain of any one of SEQ ID NOS:69-92, 222-252, and 286-289.

87. The isolated or recombinant polypeptide of claim 80, which polypeptide comprises an amino acid sequence of any one of SEQ ID NOS:69-92, 222-252, and 286-289.

88. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide has a CTLA-4/CD28BP binding affinity ratio greater than the CTLA-4/CD28BP binding affinity ratio of human B7-1.

89. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide has either a same binding affinity or an enhanced binding affinity for CTLA-4 as compared to a binding affinity of a wild type co-stimulatory molecule for CTLA-4.

90. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide has a decreased or a lowered binding affinity for CD28 as compared to a binding affinity of a wild type co-stimulatory molecule for CD28.

91. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide inhibits T-cell proliferation or T-cell activation or both T-cell proliferation and T-cell activation.

92. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide inhibits T-cell proliferation.

93. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide induces a T-cell response less than that of human B7-1.

94. The isolated or recombinant polypeptide of claim 80, wherein the polypeptide modulates T-cell activation, but does not induce proliferation of purified T-cells activated by soluble anti-CD3 mAbs.

95. The isolated or recombinant polypeptide of claim 84, which polypeptide comprises an extracellular domain sequence of any one of SEQ ID NOS:69-92 and 222-247.

96. The isolated or recombinant polypeptide of claim 80, which polypeptide comprises an extracellular domain sequence encoded by a coding polynucleotide sequence, the coding polynucleotide sequence selected from the group:

(a) an extracellular domain coding sequence of a polynucleotide sequence selected from any of SEQ ID NOS:22-45 and 143-173;

(b) a polynucleotide sequence that encodes the extracellular domain of a polypeptide selected from any of SEQ ID NOS:69-92, 222-252, and 286-289; and

(c) a polynucleotide sequence which hybridizes under stringent conditions over substantially the entire length of a polynucleotide sequence (a) or (b).

97. An isolated or recombinant polypeptide comprising a sequence that differs from a primate B7-1 sequence in at least one mutation selected from:

Ser 12 Pro; Leu 25 Met; Gly 27 Cys; Ser 29 Pro; Lys 40 Arg; His 52 Leu; Tyr 65 His; Glu 122 Asp; Glu 129 Lys; Thr 135 Met; Thr 164 Ala; Ser 174 Phe; Glu 196 Gly; Ala 199 Thr; Thr 210 Ala; Lys 219 Arg; Thr 234 Pro; Asp 241 Asn; Val 254 Ala; Arg 275 Lys; Arg 276 Ser; or Arg 279 Thr; the mutation being indicated relative to human B7-1 with the amino acid sequence shown in SEQ ID NO:278,

wherein said sequence does not occur in nature, and wherein said polypeptide has a CTLA-4/CD28BP binding affinity ratio equal to or greater than the CTLA-4/CD28BP binding affinity ratio of human B7-1.

98. The isolated or recombinant polypeptide of claim 97 wherein said sequence differs from said primate B7-1 sequence in at least two of said mutations.

99. The isolated or recombinant polypeptide of claim 97 wherein said primate B7-1 is human B7-1 (SEQ ID NO:278).

100. The isolated or recombinant polypeptide of claim 99, wherein said sequence differs from the human B7-1 sequence in at least two of said mutations.

101. An isolated or recombinant polypeptide comprising a sequence, said sequence having at least about 75% identity to at least one of SEQ ID NOS:263-272, or a subsequence thereof comprising the extracellular domain, wherein said sequence is not a naturally-occurring sequence, and

wherein said polypeptide has a CTLA-4/CD28BP binding affinity ratio equal to or greater than the CTLA-4/CD28BP binding affinity ratio of human B7-1.

102. An isolated or recombinant polypeptide, which polypeptide comprises a non naturally-occurring amino acid sequence encoded by a nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NOS:22-45, 143-173, 253-262, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:69-92, 222-247, 263-272, 286-289, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which hybridizes under highly stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b);

(d) a polynucleotide sequence comprising all or a fragment of (a), (b), or (c), wherein the fragment encodes a polypeptide having a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1;

(e) a polynucleotide sequence encoding a polypeptide, the polypeptide comprising an amino acid sequence which is substantially identical over at least about

150 contiguous amino acid residues of any one of SEQ ID NOS:69-92, 222-247, 263-272, 286-289, and

(f) a polynucleotide sequence encoding a polypeptide that has a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1, which polynucleotide sequence has at least about 70% identity to at least one polynucleotide sequence of (a), (b), (c), or (d).

103. The isolated or recombinant polypeptide of claim 102, the polypeptide comprising an amino acid sequence of any one of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289.

104. The isolated or recombinant polypeptide of claim 102, wherein the polypeptide has a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1.

105. The isolated or recombinant polypeptide of claim 102, wherein the polypeptide inhibits T-cell proliferation.

106. The isolated or recombinant polypeptide of claim 102, wherein the polypeptide induces a T-cell response less than that of human B7-1.

107. An isolated or recombinant polypeptide comprising a sequence according to the formula:

MGHTRRQGTSP-X12-KCPYLKFFQLLV-X25-ACL-X29-HLCSGVIHVT-X40-EVKEVATLSCGLNVSVEELAQTRIHWQKEKKMVLTM MSGDMNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYECVVLKY-X122-KDAFKR-X129-HLAEVMLSVKAD FPTPSITDFEIPPSNIRRIICS-X164-SGGFPEPHLFWLENGEELNAINTTVSQDPET-X196-LYTVSSKLDFNM TANHSFMCLI-X219-YGHLRVNQTFNWNTPKQEHFP-X241-NLLPSWA ITLISANGIFVICCLTYRFAPRCRERKSNETLRRESVCPV (SEQ ID NO:287), or a subsequence thereof comprising the extracellular domain,

wherein position X12 is Ser or Pro; position X25 is Leu or Met; position X29 is Ser or Pro; position X40 is Lys or Arg; position X122 is Glu or Asp; position X129 is Glu or Lys; position X164 is Thr or Ala; position X196 is Glu or Gly; position X219 is Lys or Arg; and position X241 is Asp or Asn.

108. The isolated or recombinant polypeptide of claim 107, which polypeptide comprises the extracellular domain of SEQ ID NO:288 or SEQ ID NO:289.

109. The isolated or recombinant polypeptide of claim 107, comprising the sequence SEQ ID NO:288 or SEQ ID NO:289.

110. The isolated or recombinant polypeptide of claim 107, wherein the polypeptide has a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1.

111. The isolated or recombinant polypeptide of claim 107, wherein the polypeptide inhibits T-cell proliferation.

112. The isolated or recombinant polypeptide of claim 107, wherein the polypeptide induces a T-cell response less than that of human B7-1.

113. An isolated or recombinant polypeptide comprising a subsequence of an amino acid sequence set forth in any of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289, wherein the subsequence is the extracellular domain of said amino acid sequence.

114. The isolated or recombinant polypeptide of claim 80, 97, 101, 102, 107, or 113, comprising a signal sequence.

115. The polypeptide of claim 114, wherein the signal sequence is selected from the signal sequence set forth in any of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289.

116. The polypeptide of claim 80, 97, 101, 102, 107, or 113, comprising a transmembrane domain sequence or a cytoplasmic domain sequence, selected from the transmembrane domain sequence or the cytoplasmic domain sequence set forth in any of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289.

117. The polypeptide of claim 80, 97, 101, 102, 107, or 113 comprising a soluble extracellular domain of a NCSM or a fragment or subsequence thereof.

118. The polypeptide of claim 80, 97, 101, 102, 107, or 113, wherein the polypeptide comprises a fusion protein comprising at least one additional amino acid sequence.

119. The polypeptide of claim 118, wherein the at least one additional amino acid sequence comprises an Ig polypeptide.

120. The polypeptide of claim 119, wherein the Ig polypeptide is a human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

121. The polypeptide of claim 80, 97, 101, 102, 107, or 113, comprising a polypeptide purification subsequence.

122. The polypeptide of claim 121, wherein the polypeptide purification subsequence is selected from: an epitope tag, a FLAG tag, a polyhistidine sequence, and a GST fusion.

123. The polypeptide of claim 80, 97, 101, 102, 107, or 113, comprising a modified amino acid.

124. The polypeptide of claim 123, wherein the modified amino acid is selected from the group consisting of: a glycosylated amino acid, a PEGylated amino acid, a farnesylated amino acid, an acetylated amino acid, a biotinylated amino acid, an amino acid conjugated to a lipid moiety, and an amino acid conjugated to an organic derivatizing agent.

125. A composition comprising at least one polypeptide of claim 124 and a pharmaceutically acceptable excipient.

126. A composition comprising at least one polypeptide of claim 80, 97, 101, 102, 107, or 113, and a pharmaceutically acceptable excipient.

127. A composition comprising:

an isolated or recombinant NCSM polypeptide comprising the amino acid sequence of SEQ ID NOS:69-92, 222-247, 263-272, 286-289, or a costimulatory fragment thereof, wherein said costimulatory fragment has a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1, and a carrier.

128. An isolated or recombinant nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NOS:22-45, 143-173, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:69-92, 222-247, 286-289, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which hybridizes under highly stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b); and

(d) a polynucleotide sequence comprising all or a fragment of (a), (b), or (c);

wherein (c) or (d) encodes a polypeptide having a non naturally-occurring sequence comprising at least one of:

Gly at position 2; Thr at position 4; Arg at position 5; Gly at position 8; Pro at position 12; Met at position 25; Cys at position 27; Pro at position 29; Leu at position 31; Arg at position 40; Leu at position 52; His at position 65; Ser at position 78; Asp at position 80; Tyr at position 87; Lys at position 120; Asp at position 122; Lys at position 129; Met at position 135; Phe at position 150; Ile at position 160; Ala at position 164; His at position 172; Phe at position 174; Leu at position 176; Asn at position 178; Asn at position 186; Glu at position 194; Gly at position 196; Thr at position 199; Ala at position 210; His at position 212; Arg at position 219; Pro at position 234; Asn at position 241; Leu at position 244; Thr at position 250; Ala at position 254; Tyr at position 265; Arg at position 266; Glu at position 273; Lys at position 275; Ser at position 276; an amino acid deletion at position 276; and Thr at position 279, wherein the position number corresponds to that of the human B7-1 amino acid sequence (SEQ ID NO:278), and wherein said polypeptide has a CTLA-4/CD28BP binding affinity ratio equal to or greater than the CTLA-4/CD28BP binding affinity ratio of human B7-1.

129. An isolated or recombinant nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NOS:253-262, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NOS:263-272, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence which hybridizes under highly stringent conditions over substantially the entire length of polynucleotide sequence (a) or (b) and encodes a polypeptide having a non naturally-occurring sequence; and

(d) a polynucleotide sequence comprising all or a fragment of (a), (b), or (c), wherein the fragment encodes a polypeptide having (i) a non naturally-occurring sequence and (ii) a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1.

130. An isolated or recombinant nucleic acid comprising a polynucleotide sequence encoding a polypeptide, the encoded polypeptide comprising an

amino acid sequence which is substantially identical over at least about 150 contiguous amino acid residues of any one of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289.

131. The nucleic acid of claim 44, wherein the encoded polypeptide is substantially identical over at least about 200 contiguous amino acid residues of any one of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289.

132. An isolated or recombinant nucleic acid comprising a nucleotide sequence coding for a polypeptide comprising the amino acid sequence set forth in any of SEQ ID NOS:69-92, 222-247, 263-272, and 286-289, or a subsequence thereof, wherein the subsequence comprises at least one of: the signal sequence of said polypeptide, the extracellular domain of said polypeptide, the transmembrane domain of said polypeptide, and the cytoplasmic domain of said polypeptide, and wherein the amino acid sequence or subsequence is a non naturally-occurring sequence.

133. The nucleic acid of claim 128, 129, 130, or 132, wherein the polypeptide has a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1.

134. The nucleic acid of claim 128, 129, 130, or 132, wherein the polypeptide has either a same binding affinity or an enhanced binding affinity for CD28 as compared to a binding affinity of a wild type co-stimulatory molecule for CD28.

135. The nucleic acid of claim 128, 129, 130, or 132, wherein the encoded polypeptide has a decreased or a lowered binding affinity for CTLA-4 as compared to a binding affinity of a wild type co-stimulatory molecule for CTLA-4.

136. The nucleic acid of claim 128, 129, 130, or 132, wherein the encoded polypeptide inhibits T-cell proliferation or T-cell activation or both T-cell proliferation and T-cell activation.

137. The nucleic acid of claim 128, 129, 130, or 132, wherein the encoded polypeptide modulates T-cell activation, but does not induce proliferation of purified T-cells activated by soluble anti-CD3 mAbs.

138. The nucleic acid of claim 128, 129, 130, or 132, wherein the nucleic acid encodes a fusion protein comprising at least one additional amino acid sequence.

139. The nucleic acid of claim 138, wherein the at least one additional amino acid sequence comprises an Ig polypeptide.

140. The nucleic acid of claim 139, wherein the Ig polypeptide is a human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

141. The nucleic acid of claim 128, 129, 130, or 132, wherein the encoded polypeptide comprises a signal sequence.

142. The nucleic acid of claim 128, 129, 130, or 132, wherein the encoded polypeptide comprises a precursor peptide.

143. The nucleic acid of claim 128, 129, 130, or 132, wherein the encoded polypeptide comprises an epitope tag sequence.

144. A cell comprising the nucleic acid of claim 128, 129, 130, or 132.

145. The cell of claim 144, wherein the cell expresses a polypeptide encoded by the nucleic acid.

146. A vector comprising the nucleic acid of claim 128, 129, 130, or 132.

147. The vector of claim 146, wherein the vector comprises a plasmid, a cosmid, a phage, a virus, or a fragment of a virus.

148. The vector of claim 146, wherein the vector is an expression vector.

149. The expression vector of claim 148, wherein the nucleic acid is operably linked to a promoter.

150. The expression vector of claim 149, further comprising a polynucleotide sequence encoding an Ig polypeptide or fragment thereof.

151. The expression vector of claim 150, wherein the Ig polypeptide is a human IgG polypeptide comprising an Fc hinge, a CH2 domain, and a CH3 domain.

152. The expression vector of claim 150, wherein the promoter is a CMV promoter.

153. The expression vector of claim 150, further comprising a BGH polyA sequence.

154. A host cell comprising the vector of claim 146.

155. A composition comprising the nucleic acid of claim 128, 129, 130, or 132, and an excipient.

156. The composition of claim 155, wherein the excipient is a pharmaceutically acceptable excipient.

157. A composition of matter comprising at least one nucleic acid of claim 128, 129, 130, or 132.

158. The composition of claim 157, wherein the composition comprises a library comprising at least about 2, 5, 10, 50 or more nucleic acids.

159. A composition produced by cleaving at least one nucleic acid of claim 128, 129, 130, or 132.

160. The composition of claim 159, wherein the cleaving comprises mechanical, chemical, or enzymatic cleavage.

161. The composition of claim 160, wherein the enzymatic cleavage comprises cleavage with a restriction endonuclease, an RNAse, or a DNAse.

162. A composition produced by a process comprising incubating at least one nucleic acid of claim 128, 129, 130, or 132 in the presence of deoxyribonucleotide triphosphates and a nucleic acid polymerase.

163. The composition of claim 162, wherein the nucleic acid polymerase is a thermostable polymerase.

164. An isolated or recombinant nucleic acid encoding a polypeptide that has a CTLA-4/CD28 binding affinity ratio equal to or greater than the CTLA-4/CD28 binding affinity ratio of human B7-1, produced by mutating or recombining at least one nucleic acid of claim 128, 129, 130, or 132.

165. An isolated or recombinant polypeptide comprising a sequence according to the formula:

MGHTMKWGSLPPKRPCLWLSQLLVLTGLFYFCSGITPK SVTKRVKETVM-X50-SCDY-X55-X56-STEELTSLRIYWQKDSKMVL AILPGKVQVWPEYKNRTITD MNDNPRIVILALRLSD-X113-GTYTCV-X120-QK-X123-X124-X125-X126-G-X128-X129-X130-X131-EHL-X135-SV-X138-L-X140-

IRADFPVPSITDIGHPAPNVK RIRCSASG-X170-FPEPRLAWMEDGEEL NAVNTTV-X193-X194-X195-LDTELYSVSSELD-X209-N-X211-TNNHSIVCLIKYGELSVSQIFPWSKPK QEPPIDQLPFWVI-X252-X253-VSGALVLTAVVLYCLACRHVAR (SEQ ID NO:290), or a subsequence thereof comprising the extracellular domain,

wherein position X50 is Leu or Pro; position X55 is Asn or Ser; position X56 is Ala or Thr; position X113 is Ser or Lys; position X120 is Ile or Val; position X123 is Pro or deleted; position X124 is Val, Asn, or Asp; position X125 is Leu or Glu; position X126 is Lys or Asn; position X128 is Ala or Ser; position X129 is Tyr or Phe; position X130 is Lys or Arg; position X131 is Leu or Arg; position X135 is Ala or Thr; position X138 is Arg or Thr; position X140 is Met or Ser; position X170 is Asp or Gly; position X193 is Asp or is deleted; position X194 is Gln or is deleted; position X195 is Asp or is deleted; position X211 is Val or Ala; position X252 is Ile or Val; and position X253 is Leu or Pro.

166. The isolated or recombinant polypeptide of claim 165, which polypeptide comprises a sequence of any one of SEQ ID NOS:59, 62, 180, 184, 188, 195, 196, 200, 201, 204, 211, 213, 219, and 291.

167. An isolated or recombinant polypeptide comprising a sequence according to the formula:

MGHTMKWG-X9-LPPKRPCLWLSQLLVLTGLFYFCSG-X35-TPKSVTKRV KETVMLSCDY-X55-TSTEELTSLRIYWQKDSKMVLAILPGKVQVW PEYKNRTITDMNDNPRIVILALR-X110-SDSGTYTCVIQKP-X124-LKGAYKLEHL-X135-SVRLMIRADFPVPTINDLGNPSPNIRRLICSTSGGFPRPHLYWLENG-X183-ELNATNTT-X192-SQDPETKLYMISSELDFN-X211-TSN-X215-X216-X217-LCLVKYGDLTVSQ-X231-FYWQESKPTPSANQHLTWTIIIPVSAFGISVIIAVI LTCLTCRNAAIRRQRRENEV-X288-M-X290-SCSQSP (SEQ ID NO:292), or a subsequence thereof comprising the extracellular domain,

wherein position X9 is Thr or Ser; position X35 is Ile or Thr; position X55 is Asn or Ser; position X110 is Leu or Pro; position X124 is Asp or Val; position X135 is

Thr or Ala; position X183 is Lys or Glu; position X192 is Leu or Val; position X211 is Met or Thr; position X215 is His or is deleted; position X216 is Ser or is deleted; position X217 is Phe or is deleted; position X231 is Thr or Ser; position X288 is Lys or Glu; position X290 is Glu or Gln, and wherein said sequence is a non naturally-occurring sequence.

168. The isolated or recombinant polypeptide of claim 167, which polypeptide comprises a sequence of any one of SEQ ID NOS:48, 182, 183, 212, 214, 216, 218, 221, and 293.

169. An isolated or recombinant polypeptide comprising the sequence SEQ ID NO:93, SEQ ID NO:94, or a subsequence thereof, wherein the subsequence comprises at least one of: the signal sequence of said polypeptide, the extracellular domain of said polypeptide, the transmembrane domain of said polypeptide, and the cytoplasmic domain of said polypeptide.

170. An isolated or recombinant nucleic acid comprising a polynucleotide sequence selected from:

(a) a polynucleotide sequence selected from SEQ ID NO:46, SEQ ID NO:47, or a complementary polynucleotide sequence thereof;

(b) a polynucleotide sequence encoding a polypeptide selected from SEQ ID NO:93, SEQ ID NO:94, or a complementary polynucleotide sequence thereof;

(c) a polynucleotide sequence encoding a subsequence of a polypeptide selected from SEQ ID NO:93, SEQ ID NO:94, or a complementary polynucleotide sequence thereof, wherein the subsequence comprises at least one of: the signal sequence of said polypeptide, the extracellular domain of said polypeptide, the transmembrane domain of said polypeptide, and the cytoplasmic domain of said polypeptide.

171. A polypeptide which is specifically bound by a polyclonal antisera raised against one or more antigen, the antigen comprising the sequence SEQ ID NOS:48-94, 174-252, 263-272, 283-293, or a fragment thereof, wherein the antisera is

subtracted with a polypeptide encoded by one or more of GenBank Nucleotide Accession Nos: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442, AF203443, AF216747, AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950.

172. An antibody or antisera produced by administering the polypeptide of claim 1, 80, 101, or 169 to a mammal, which antibody specifically binds one or more antigen, the antigen comprising a polypeptide comprising one or more of the amino acid sequences SEQ ID NOS:48-94, 174-252, 263-272, and 283-293, which antibody does not specifically bind to a polypeptide encoded by one or more of GenBank Nucleotide Accession Nos: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442, AF203443, AF216747, AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950.

173. An antibody or antisera which specifically binds a polypeptide, the polypeptide comprising a sequence selected from: SEQ ID NOS:48-94, 174-252, 263-272, and 283-293, wherein the antibody does not specifically bind to a polypeptide encoded by one or more of GenBank Nucleotide Accession Nos: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442,

AF203443, AF216747, AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950.

174. A method of producing a polypeptide, the method comprising:

(a) introducing into a population of cells a nucleic acid of claim 43, 46, 128, 129, 132, or 170, the nucleic acid operatively linked to a regulatory sequence effective to produce the encoded polypeptide;

(b) culturing the cells in a culture medium to produce the polypeptide; and

(c) isolating the polypeptide from the cells or from the culture medium.

175. A method of producing a polypeptide, the method comprising

(a) introducing into a population of cells a recombinant expression vector comprising the nucleic acid of claim 43, 46, 128, 129, 132, or 170;

(b) culturing the cells in a culture medium to produce the polypeptide encoded by the expression vector; and

(c) isolating the polypeptide from the cells or from the culture medium.

176. A method of producing a polypeptide, the method comprising:

(a) introducing into a population of cells a recombinant expression vector comprising the nucleic acid of claim 43, 46, 128, 129, 132, or 170;

(b) administering the expression vector into a mammal; and

(c) isolating the polypeptide from the mammal or from a byproduct of the mammal.

177. A method of inducing T-cell proliferation, the method comprising: contacting the T-cell population with a polypeptide of claim 1, 80, 101, or 169, thereby inducing proliferation of the T-cells.

178. A method of inhibiting T-cell proliferation, the method comprising: contacting the T-cell population with a polypeptide of claim 1, 80, 101, or 169, thereby inhibiting proliferation of the T-cells.

179. A method of modifying T-cell proliferation, the method comprising: contacting the T-cell population with a polypeptide of claim 1, 80, 101, or 169, thereby modifying proliferation of the T-cells.

180. A method of modifying T-cell activation, the method comprising: contacting the T-cell population with a polypeptide of claim 1, 80, 101, or 169, thereby modifying activation of the T-cells.

181. The method of claim 177, 178, 179, or 180 wherein the T-cells are in culture.

182. A method of treating an autoimmune disorder or medical condition in a patient, the method comprising: administering to the patient an effective amount of the polypeptide of claim 1, 80, 101, or 169.

183. A method of treating an autoimmune disorder or medical condition in a patient, the method comprising: administering to the patient an appropriate amount of an expression vector comprising the nucleic acid of claim 1, 80, 101, or 169.

184. The method of claim 182, wherein the autoimmune disorder is selected from the group comprising: multiple sclerosis, rheumatoid arthritis, lupus erythematosus, psoriasis, and type I diabetes.

185. The method of claim 182, wherein the medical condition comprises allogeneic or xenogeneic grafts or transplants.

186. A method of treating a medical disorder in a patient, the method comprising: administering to the patient an effective amount of the polypeptide of claim 1, 80, 101, or 169.

187. The method of claim 186, wherein the medical condition comprises: cancer, viral infection (e.g. HIV), or bacterial infection.

188. In a method of treating a disorder treatable by administration of a co-stimulatory molecule to a subject, an improved method comprising: administering to the subject an effective amount of the polypeptide of claim 1, 80, 101, or 169.

189. The method of claim 188, wherein the disorder treatable by administration of a co-stimulatory molecule is selected from the group comprising: sclerosis, rheumatoid arthritis, lupus erythematosus, psoriasis, type I diabetes, allogeneic grafts, xenogeneic grafts, cancer, viral infection, and bacterial infection.

190. A method of recombination, the method comprising recursively recombining one or more nucleic acid of claim 43, 46, 128, 129, 132, or 170, with one or more additional nucleic acid.

191. The method of claim 190, wherein the additional nucleic acid encodes a co-stimulatory homologue or subsequence thereof.

192. The method of claim 190, wherein the recursive recombination produces at least one library of recombinant co-stimulatory homologue nucleic acids.

193. A nucleic acid library produced by the method of claim 192.

194. A population of cells comprising the library of claim 193.

195. A recombinant co-stimulatory homologue nucleic acid produced by the method of claim 191.

196. A cell comprising the nucleic acid of claim 195.

197. The method of claim 190, wherein the recursive recombination is performed in vitro.

198. The method of claim 190, wherein the recursive recombination is performed in vivo.

199. A method of producing a modified co-stimulatory nucleic acid homologue comprising mutating a nucleic acid of claim 43, 46, 128, 129, 132, or 170.

200. The modified co-stimulatory homologue nucleic acid homologue produced by the method of claim 199.

201. A computer or computer readable medium comprising a database comprising a sequence record comprising one or more character string corresponding to a nucleic acid or protein sequence selected from SEQ ID NOS:1-272 and 283-293.

202. An integrated system comprising a computer or computer readable medium comprising a database comprising one or more sequence records, each comprising one or more character strings corresponding to a nucleic acid or protein sequence selected from SEQ ID NOS:1-272 and 283-293, the integrated system further comprising a user input interface allowing a user to selectively view one or more sequence record.

203. The integrated system of claim 202, the computer or computer readable medium comprising an alignment instruction set which aligns the character

strings with one or more additional character string corresponding to a nucleic acid or protein sequence.

204. The integrated system of claim 203, wherein the instruction set comprises one or more of: a local homology comparison determination, a homology alignment determination, a search for similarity determination, and a BLAST determination.

205. The integrated system of claim 203, further comprising a user readable output element which displays an alignment produced by the alignment instruction set.

206. The integrated system of claim 202, the computer or computer readable medium further comprising an instruction set which translates one or more nucleic acid sequence comprising a sequence selected from SEQ ID NOS:1-47, 95-173, and 253-262 into an amino acid sequence.

207. The integrated system of claim 202, the computer or computer readable medium further comprising an instruction set for reverse-translating one or more amino acid sequence comprising a sequence selected from SEQ ID NOS:48-94, 174-252, 263-272, and 283-293, into a nucleic acid sequence.

208. The integrated system of claim 207, wherein the instruction set selects the nucleic acid sequence by applying a codon usage instruction set or an instruction set which determines sequence identity to a test nucleic acid sequence.

209. A method of using a computer system to present information pertaining to at least one of a plurality of sequence records stored in a database, said sequence records each comprising one or more character string corresponding to SEQ ID NOS:1-272 and 283-293, the method comprising:

(a) determining a list of one or more character strings corresponding to one or more of SEQ ID NOS:1-272 and 283-293, or a subsequence thereof;

(b) determining which character strings of said list are selected by a user; and

(c) displaying the selected character strings, or aligning the selected character strings with an additional character string.

210. The method of claim 209, further comprising displaying an alignment of the selected character string with the additional character string.

211. The method of claim 209, further comprising displaying the list.

212. A nucleic acid which comprises a unique subsequence in a nucleic acid selected from SEQ ID NOS:1-47, 95-173, and 253-262, wherein the unique subsequence is unique as compared to a nucleic acid corresponding to any of GenBank Nucleotide Accession No.: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442, AF203443, AF216747, AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950.

213. A polypeptide which comprises a unique subsequence in a polypeptide selected from: SEQ ID NOS:48-94, 174-252, 263-272, and 283-293, wherein the unique subsequence is unique as compared to a polypeptide encoded by any of GenBank Nucleotide Accession Nos: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442, AF203443, AF216747,

AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950.

214. A target nucleic acid which hybridizes under stringent conditions to a unique coding oligonucleotide which encodes a unique subsequence in a polypeptide selected from: SEQ ID NOS:48-94, 174-252, 263-272, and 283-293, wherein the unique subsequence is unique as compared to a polypeptide encoded by any of GenBank Nucleotide Accession No.: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442, AF203443, AF216747, AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950.

215. The nucleic acid of claim 214, wherein the stringent conditions are selected such that a perfectly complementary oligonucleotide to the coding oligonucleotide hybridizes to the coding oligonucleotide with at least about a 5x higher signal to noise ratio than for hybridization of the perfectly complementary oligonucleotide to a control nucleic acid corresponding to any of GenBank Nucleotide Accession No.: A92749, A92750, AA983817, AB026121, AB030650, AB030651, AB038153, AF010465, AF065893, AF065894, AF065895, AF065896, AF079519, AF106824, AF106825, AF106828, AF106829, AF106830, AF106831, AF106832, AF106833, AF106834, AF203442, AF203443, AF216747, AF257653, AH004645, AH008762, AX000904, AX000905, D49843, L12586, L12587, M27533, M83073, M83074, M83075, M83077, NM005191, S74541, S74540, S74695, S74696, U05593, U10925, U19833, U19840, U26832, U33063, U33208, U57755, U88622, X60958, Y08823, and Y09950, wherein the target nucleic acid hybridizes to the unique coding

oligonucleotide with at least about a 2x higher signal to noise ratio as compared to hybridization of the control nucleic acid to the coding oligonucleotide.

216. A method of therapeutic or prophylactic treatment of a disease or disorder in a subject in need of such treatment, comprising: administering to the subject a polypeptide of claim 1, 80, 101, or 169 and an immunogen specific for said disease or disorder, wherein the combined amount of polypeptide and immunogen is effective to prophylactically or therapeutically treat said disease or disorder.

217. The method of claim 216, wherein the polypeptide is present in an amount sufficient to enhance, diminish or modify an immune response induced by the immunogen.

218. The method of claim 216, wherein a composition comprising the polypeptide, the immunogen, and a pharmaceutically acceptable excipient is administered to the subject in an amount effective to treat said disease or disorder.

219. The method of claim 216, wherein the subject is a mammal.

220. The method of claim 219, wherein the mammal is a human.

221. The method of claim 216, wherein the polypeptide is administered in vivo to the subject.

222. The method of claim 216, wherein the polypeptide is administered in vitro or ex vivo to one or more cells of the subject.

223. A method of enhancing, diminishing, modifying, or potentiating an immune response in a subject, comprising: directly administering to the subject a polynucleotide comprising a nucleic acid sequence of claim 43, 46, 128, 129, 132, or 170, operably linked to a promoter sequence that controls the expression of said nucleic acid

sequence, said polynucleotide being present in an amount sufficient that uptake of said polynucleotide into one or more cells of the subject occurs and sufficient expression of said nucleic acid sequence results to produce an amount of a polypeptide effective to enhance, diminish, or modify an immune response.

224. The method of claim 223, further comprising administering to the subject an antigen specific for the disease or disorder, wherein the polynucleotide is administered to the subject in an amount sufficient to enhance, diminish, or modify the immune response induced in the subject by the antigen.

225. The method of claim 223, wherein the polynucleotide further comprises a nucleotide sequence encoding for an antigen.

226. The method of claim 223, wherein the polynucleotide further comprises at least one additional nucleotide sequence encoding a cytokine, adjuvant, co-stimulatory molecule, or at least one additional nucleotide sequence comprising a promoter.

227. The method of claim 223, wherein the subject is a mammal.

228. The method of claim 227, wherein the mammal is a human.

229. The method of claim 223, wherein said polynucleotide comprises a vector.

230. A method of treating a disease or disorder in a subject in need of such treatment, comprising: administering to the subject a polypeptide of claim 1, 80, 101, or 169 in an amount effective to treat said disease or disorder.

231. A method of therapeutic or prophylactic treatment of a disease or disorder in a subject in need of such treatment, comprising: administering to the subject a

polypeptide of claim 32 or 117 and an immunogen specific for said disease or disorder, wherein the combined amount of polypeptide and immunogen is effective to prophylactically or therapeutically treat said disease or disorder.

232. The method of claim 231, wherein the polypeptide is present in an amount sufficient to enhance, diminish or modify an immune response induced by the immunogen.

233. The method of claim 231, wherein a composition comprising the polypeptide, the immunogen, and a pharmaceutically acceptable excipient is administered to the subject in an amount effective to treat the disease or disorder.

234. The method of claim 231, wherein the subject is a mammal.

235. The method of claim 234, wherein the mammal is a human.

236. The method of claim 231, wherein the polypeptide is administered in vivo to the subject.

237. The method of claim 231, wherein the polypeptide is administered in vitro or ex vivo to one or more cells of the subject.

238. A method of treating a disease or disorder in a subject in need of such treatment, comprising: administering to the subject a polypeptide of claim 58 in an amount effective to treat the disease or disorder.

239. The isolated or recombinant polypeptide of claim 165, comprising three or more of:

Leu at position X50; Asn at position X55; Ala at position X56; Ser at position X113; Ile at position X120; Pro at position X123; Val at position X124; Leu at position X125; Lys at position X126; Ala at position X128; Tyr at position X129; Lys at

position X130; Leu at position X131; Ala at position X135; Arg at position X138; Met at position X140; Asp at position X170; Asp at position X193; Asp at position X194; Asp at position X195; Val at position X211; Ile at position X252; and Leu at position X253.

240. The isolated or recombinant polypeptide of claim 167, comprising three or more of:

Thr at position X9; Ile at position X35; Asn at position X55; Leu at position X110; Asp at position X124; Thr at position X135; Lys at position X183; Leu at position X192; Met at position X211; His at position X215; Ser at position X216; Phe at position X217; Thr at position X231; Lys at position X288; and Glu at position X290.

241. A method of modulating or altering a T-cell response specific to an antigen in a subject, the method comprising administering to the subject at least one polynucleotide sequence encoding a polypeptide comprising any of SEQ ID NOS:48-94, 174-252, 263-272 and 283-293 or fragment thereof, and a polynucleotide sequence encoding the antigen or antigenic fragment thereof, wherein each of the at least one polynucleotide sequences is expressed in the subject in an amount effective to modulate or alter a T cell response.

242. The vector of claim 241, wherein the at least one polynucleotide sequence encoding a polypeptide comprises a polynucleotide sequence selected from any of SEQ ID NOS:1-47, 95-173, and 253-262.

243. The method of claim 241, wherein the polypeptide or fragment thereof interacts with or binds a T cell surface receptor.

244. The method of claim 241, wherein the T-cell response is enhanced.

245. The method of claim 244, wherein the enhanced T cell response is sufficient to eliminate cells bearing the antigen or antigenic fragment thereof.

246. The method of claim 241, wherein the T-cell response is suppressed or inhibited.

247. The method of claim 241, wherein the antigen or antigenic fragment thereof is an antigen or antigenic fragment thereof of an infectious agent or a cancer.

248. The method of claim 244, wherein the polypeptide comprises SEQ ID NO:66 or the extracellular domain amino acid sequence thereof.

249. The method of claim 245, wherein the polypeptide comprises SEQ ID NO:86 or the extracellular domain amino acid sequence thereof.

250. The method of claim 244, wherein the at least one polynucleotide sequence encoding a NCSM polypeptide or fragment thereof is operably linked to a promoter in a first vector.

251. The method of claim 250, wherein the at least one polynucleotide sequence encoding the antigen or antigenic fragment thereof is operably linked to a promoter in the first vector.

252. The method of claim 250, wherein the at least one polynucleotide sequence encoding the antigen or antigenic fragment thereof is operably linked to a promoter in the a second vector.

253. A vector comprising at least one polynucleotide sequence encoding a polypeptide comprising any of SEQ ID NOS:48-94, 174-252, 263-272 and 283-293 or fragment thereof, and a polynucleotide sequence encoding the antigen or antigenic fragment thereof, wherein the NCSM polypeptide or fragment thereof interacts with or binds to a T cell receptor when expressed in a subject, and wherein each of the at least one polynucleotide sequences is operably linked to a promoter for expression in the subject and is present in an amount sufficient that when expressed is effective to modulate or alter a T cell response.

254. The vector of claim 253, wherein the at least one polynucleotide sequence encoding a polypeptide comprises a polynucleotide sequence of any of SEQ ID NOS:1-47, 95-173, and 253-262.

255. The vector of claim 253, wherein each of the at least one polynucleotide sequences is expressed in the subject in an amount effective to enhance a T cell response such that cells expressing the antigen or antigenic fragment thereof are eliminated.

256. The vector of claim 253, wherein each of the at least one polynucleotide sequences is expressed in the subject in an amount effective to inhibit a T cell response.

257. A vector comprising at least one polynucleotide sequence encoding a polypeptide comprising any of SEQ ID NOS:48-94, 174-252, 263-272 and 283-293 or fragment thereof, wherein the polypeptide or fragment thereof interacts with or binds to a T cell receptor when expressed in a subject, wherein the at least one polynucleotide sequence is operably linked to a promoter for expression in the subject and is present in an amount sufficient that when expressed is effective to modulate or alter a T cell response.

258. A method of modulating or altering an immune response in a subject, the method comprising introducing into cells of a tumor of the subject at least one polynucleotide sequence encoding a polypeptide comprising any of SEQ ID NOS:48-94, 174-252, 263-272 and 283-293 or fragment thereof, wherein the polypeptide or fragment thereof interacts with or binds to a T cell receptor when expressed in a subject, and wherein the at least one polynucleotide sequence is operably linked to a promoter for expression in the subject and is present in an amount sufficient that when expressed is effective to modulate or alter a T cell response.